

SUPPLEMENTAL DIGITAL CONTENT

Factors Associated with Diagnostic Error on Admission to a Pediatric Intensive Care Unit: A Pilot Study

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1. Safer Dx Instrument

The Safer Dx Instrument is a validated tool to determine occurrence of diagnostic error (DE) using structured chart review (1, 2). The following is the instrument as it appeared in data collection forms used for this study.

SAFER DX INSTRUMENT						
For the episode of care under review (first 12 hours after PICU admission), rate your agreement with the following items.						
Rate each item on a scale of 1 to 6, with 1 = Strongly Agree and 6 = Strongly Disagree						
	1 Strongly Agree	2	3	4	5	6 Strongly Disagree
1. Based on patient history that was documented during the first 12 hours after PICU admission, an opportunity to make the subsequent final diagnosis was missed.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2. Based on patient physical exam that was documented during the first 12 hours after PICU admission, an opportunity to make the subsequent final diagnosis was missed.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3. Based on diagnostic data (laboratory, radiology, pathology or other results) that were available or documented during the first 12 hours after PICU admission, an opportunity to make the subsequent final diagnosis was missed.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4. The diagnostic process during the first 12 hours after PICU admission was affected by incomplete or incorrect clinical information given to the care team by patient or caregiver.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
5. The clinical information (i.e., history, physical exam and diagnostic data) present during the first 12 hours after PICU admission should have prompted additional diagnostic evaluation through tests or consults.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

6. The initial assessment at the end of the first 12 hours after PICU admission was appropriate, given the patient's medical history and clinical presentation.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
7. Alarm symptoms or "red flags" (i.e., features in the clinical presentation that are considered to predict serious disease) were not acted upon during the first 12 hours after PICU admission.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
8. Diagnostic data (laboratory, radiology, pathology or other results) available or documented during the first 12 hours after PICU admission were misinterpreted in relation to the subsequent final diagnosis.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
9. The differential diagnosis documented during the first 12 hours after PICU admission included the subsequent final diagnosis.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
10. The final diagnosis was an evolution of the initial presumed diagnosis.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
11. The clinical presentation was atypical, given the final diagnosis.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
12. In conclusion, based on the above questions, the episode of care under review (first 12 hours after PICU admission) had a diagnostic error.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

2. Sample Size Calculations

Our pilot study (n=50) estimated 8% of patients had at least one DE within the first 12 hours of PICU admission. To determine the association of specific patient, provider, and work system factors with DE, we calculated the minimum sample size needed (80% power at $\alpha=0.05$) for selected predictor variables while accounting for clustering of DE by provider (see below). We determined that 610 PICU admissions was the largest among these, thus a sample size of 610 would provide sufficient power for all variables (**Table**). Note that we estimated expected effect sizes per variable based on our pilot study except for mortality, which was based on existing literature reporting a 5-12% mortality difference between critically ill patients with vs. without DE, with more deaths noted among patients with DE (3, 4).

Given potential clustering of DE by provider (non-independence), the estimated sample size was inflated by 15%. This inflation factor was calculated using a statistical formula (5) considering a cluster size coefficient of variation of 0.5, an average cluster size of 10-50, and an intra-cluster correlation coefficient of ≤ 0.1 (from pilot data). Sample size calculations were performed using SAS 9.4 ©2017 (SAS Institute, Inc., Cary, NC, 2017).

For the full study, we plan to use generalized linear mixed models (GLMM) with random effects at the provider and site level to estimate the odds of DE (outcome

variable) given specific patient, provider, and work system/site factors (predictor variables).

Table. Sample Size Calculations to Determine Associations with Diagnostic Error

Predictor Covariates	With Diagnostic Error	No Diagnostic Error	Estimated Effect Size*	Sample Size	Adjusted Sample Size**
PRISM III score, median***	0.735	0.505	0.23	88	102
Chief complaint category, % neurologic	75%	20%	55%	60	69
Presence of change in diagnosis, %	50%	20%	30%	190	219
Patient outcome, % mortality	15%	4%	11%	530	610
Admission source, % referral from other institution	95%	43%	52%	70	81
Admission time, % night shift	95%	37%	58%	50	58
Any subspecialty consults within 1st 24 hours, %	5%	41%	-36%	120	138

*Based on pilot study (n=50) except for mortality, which was based on published mortality differences between patients with vs. without diagnostic error.

**Sample sizes were multiplied by 1.15 (inflation factor of 15%) to account for potential clustering of diagnostic error by provider, allowing for an intra-cluster correlation coefficient of up to 10%.

***PRISM III - Pediatric Risk of Mortality III score is an estimate of the % probability of death on admission

References for Supplemental Digital Content

1. Al-Mutairi A, Meyer AND, Thomas EJ, et al.: Accuracy of the Safer Dx Instrument to Identify Diagnostic Errors in Primary Care. *J Gen Intern Med* 2016; 31:602–608
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3. Hautz SC, Schuler L, Kämmer JE, et al.: Factors predicting a change in diagnosis in patients hospitalised through the emergency room: a prospective observational study. *BMJ Open* 2016; 6:e011585
4. Cifra CL, Jones KL, Ascenzi JA, et al.: Diagnostic Errors in a PICU: Insights From the Morbidity and Mortality Conference. *Pediatr Crit Care Med* 2015; 16:468–476
5. Eldridge SM, Ashby D, Kerry S: Sample size for cluster randomized trials: effect of coefficient of variation of cluster size and analysis method. *Int J Epidemiol* 2006; 35:1292–1300